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10/580,856	11/21/2006	Jacques Defaye	0508-1163	5988

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EXAMINER	
LAU, JONATHAN S	
ART UNIT	PAPER NUMBER
1623	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,856	DEFAYE ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 Apr 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-43* is/are pending in the application.

4a) Of the above claim(s) *21-34,38,40 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-37,39,41 and 43* is/are rejected.

7)☒ Claim(s) *35-37, 39, 41 and 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3,pg / 26 May 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is the national stage entry of PCT/FR04/02998, filed 24 Nov 2004; and claims benefit of foreign priority document FRANCE 0323873, filed 26 Nov 2003. An English language translation of this foreign priority document is of record.

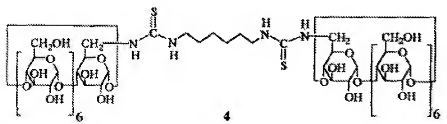
Claims 21-43 are pending in the current application. Claims 21-34, 38, 40 and 42, drawn to non-elected inventions, are withdrawn. Claims 35-37(in part), 39 (in part), 41 (in part) and 43 (in part) are examined on the merits herein.

Election/Restrictions

Applicant's election with traverse of the invention of Group III, claims claim(s) 35-37(in part), 39 (in part), 41 (in part) and 43 (in part), in the reply filed on 14 Apr 2008 is acknowledged. The traversal is on the ground(s) that the applied reference, Benito et al. (J. Am. Chem. Soc., 2004, 126, p10355-10363, of record) does not constitute prior art. This is found persuasive because the English translation of foreign priority document FRANCE 0323873, filed 14 Apr 2008, provides support for the instantly claimed invention.

However, it is found that the inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The common feature of the inventions of Groups I-IV is the cyclodextrin dimer corresponding to the general formula (I). However, such a cyclodextrin dimer is a known compound. Charbonnier et al. (Tetrahedron Letters, 1999, 40, p6581-6583,

cited in PTO-892) discloses such a cyclodextrin dimer:



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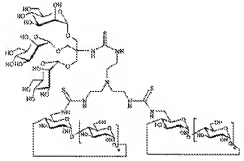
(page 6583, compound 4 in scheme 1). This compound 4 is a compound of the formula (I) disclosed in instant claim 21 in which m is 6, A is hydrogen, Y is –NH-, X is S, W is CH, Z is hydrogen, and n is 1 to 4 and n' is equal to (5-n), or 4 to 1.

Therefore said cyclodextrin dimer is not the special technical feature of a single general inventive concept. The special technical feature of Group I is the specific chemical structure of a specific cyclodextrin dimer corresponding to the general formula (I) containing a specific biological recognition element. The special technical feature of Group II is the specific chemical structure of a specific cyclodextrin dimer corresponding to the general formula (I) not containing a biological recognition element. The special technical feature of Group III is the specific chemical structure of a complex of a specific pharmacologically active agent and a specific cyclodextrin dimer corresponding to the general formula (I) containing a biological recognition element. The special technical feature of Group III is the specific chemical structure of a complex of a specific pharmacologically active agent and a specific cyclodextrin dimer corresponding to the general formula (I) not containing a biological recognition element.

The finding of Lack of Unity is still deemed proper. This finding of Lack of Unity is based on the reasons discussed above, and therefore not made final.

Claims 21-34, 38, 40 and 42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 14 Apr 2008.

Applicant's provisional election of species with traverse of the compound 6, bis[2-[N'-(6^1-deoxycyclomaltoheptaos-6^1-yl)thioureido]ethyl] 2- [N'-[tris(2,3,4,6-tetra-O-acetyl-alpha-D-mannopyranosyloxy- methyl)methyl]thioureido]ethylamine



, in the reply filed on 14 Apr 2008 is acknowledged. The traversal is on the ground(s) that the applied reference, Benito et al. (J. Am. Chem. Soc., 2004, 126, p10355-10363, of record) does not constitute prior art. This is found persuasive because the English translation of foreign priority document FRANCE 0323873, filed 14 Apr 2008, provides support for the instantly claimed invention.

As recited above, based on new grounds it is found that the inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. The special technical feature is as recited above.

The finding of Lack of Unity is still deemed proper. This finding of Lack of Unity is based on the reasons discussed above, and therefore not made final.

Claim Objections

Claims 35-37, 39, 41 and 43 are objected to because of the following informalities: Claims 35-37, 39, 41 and 43 recite within each claim multiple distinct inventions as detailed in the Requirement for Restriction mailed 13 Feb 2008. Claim 21, from which claims 35-37, 39, 41 and 43 depend, recites the invention of both Group I and Group II. Claims 35-37, 39, 41 and 43, because they depend from claim 21 and incorporate all limitations therein, recite the invention of both Group III and Group IV.

Claim 41 is further objected to for failing to end in a period.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-37, 39, 41 and 43 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 21 recites **derivatives** of an aromatic group (page 4, line 8) and an amino acid **derivative** (page 4,

line 13). Claims 35-37, 39, 41 and 43 depend from claim 21 and incorporate all limitations therein.

The specification discloses chemical groups, such as a phenyl group carrying substituents on the aromatic ring such as the methyl, ethyl, chlorine, bromine, iodine, nitro, hydroxyl, methoxyl or acetamido substituents (page 5, lines 20-25) and an amino acid (page 5, line 25) which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 35-37, 39, 41 and 43 are directed to encompass a chemical containing derivative groups, which only correspond in some undefined way to specifically instantly disclosed chemical groups. None of these derivatives meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and because chemical derivatives are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim. No limiting definition of derivative is provided, and the example provided does not limit a derivative of an aromatic group to one carrying substituents on the aromatic ring such as the methyl, ethyl, chlorine, bromine, iodine, nitro, hydroxyl, methoxyl or acetamido substituents.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that

[he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed derivatives, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the structurally defined chemical compounds, but not the full breadth of the claims, meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear

that the written description provision of 35 USC § 112 is severable from its enablement provision. (See Vas-Cath at page 1115.)

The court of *In re Curtis* held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when... the evidence indicates ordinary artisans could not predict the operability ... of any other species." (see *In re Curtis* 354 F.3d 1347, 69 USPQ2d 1274, Fed. Cir. 2004). The court of *Noelle v. Lederman* also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, and no description of human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown" failed. See 355 F.3d 1343, 69 USPQ2d 1508, Fed. Cir. 2004.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35-37, 39, 41 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 35-37, 39, 41 and 43, which depend from claim 21 and incorporate all limitations therein, the phrase "such as" in claim 21, on page 4 lines 3, 9 and 12-13 of the claims, renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP

§ 2173.05(d). Claims 35-37, 39, 41 and 43 depend from claim 21 and incorporate all limitations therein, including the phrase "such as".

Regarding specifically claim 36, the phrase "such as" and "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 103

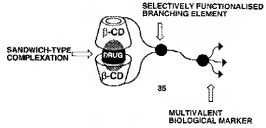
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

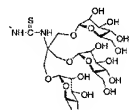
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ortiz-Mellet et al. (Chem. Eur. J. 2002, 8(9), p1982-1990, cited in PTO-892) in view of Kotter et al. (J. Chem. Soc., Perkin Trans. 1, 1998, p2193-2200, cited in PTO-892).

Ortiz-Mellet et al. discloses conjugates of a cyclodextrin dimer linked by a

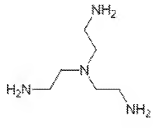


branching element to a biological marker, (page 1989, left column, structure 35 in Figure 4). Ortiz-Mellet et al. discloses the structure as a drug delivery system forming a 2:1 host-guest complex (page 1989, left column, paragraph 2). Ortiz-Mellet et al. discloses using the anticancer drug taxotere, a drug of the taxol family, as the guest compound (page 1989, left column, paragraph 1). Ortiz-



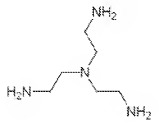
Mellet et al. discloses the biological marker moiety (page 1988, right column, scheme 7). Ortiz-Mellet et al. discloses it is advantageous that long enough spacer arms are used to warrant the accessibility of the glycocluster structure to carbohydrate-lectin recognition events and that substitution with numerous biological marker moieties may also impair inclusion and stabilization of potential guests (page 1988, right column, paragraph 1).

Ortiz-Mellet et al. does not specifically disclose the compound bis[2-[N'-(6^1-deoxycyclomaltoheptaos-6^1-yl)thioureido]ethyl] 2-[**N'**-[tris(2,3,4,6-tetra-O-acetyl-alpha-D-mannopyranosyloxy- methyl)methyl]thioureido]ethylamine (compound no. 6).



Kotter teaches the compound is a branching element known to be useful as a linker between saccharide moieties (column 2195, right column, scheme 5). Kotter teaches the compound is a linker useful in the field of carbohydrate protein interactions (page 2193, abstract and left column, paragraph 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Ortiz-Mellet et al. in view of Kotter et al. Both Ortiz-Mellet et al. and Kotter et al. are drawn to the field of branching agents to link saccharide moieties for carbohydrate protein interactions. It is *prima facie* obvious to substitute the equivalent known for the same purpose of the branching element compound



taught by Kotter et al. for the branching element disclosed by Ortiz-Mellet et al. One of ordinary skill in the art would be motivated to combine Ortiz-Mellet et al. in view of Kotter et al. because Ortiz-Mellet et al. discloses it is

advantageous that long enough spacer arms are used to warrant the accessibility of the glycocluster structure to carbohydrate - lectin recognition events.

Claims 39, 41 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ortiz-Mellet et al. (Chem. Eur. J. 2002, 8(9), p1982-1990, cited in PTO-892) in view of Kotter et al. (J. Chem. Soc., Perkin Trans. 1, 1998, p2193-2200, cited in PTO-892) as applied to claims 35-37 above, and further in view of Hamada et al. (US Patent 5,684,169, issued 04 Nov 1997, cited in PTO-892).

Ortiz-Mellet et al. in view of Kotter et al. teaches as above.

Ortiz-Mellet et al. in view of Kotter et al. does not specifically teach a pharmaceutical composition comprising said compound no 6, or said composition in the form of an aqueous solution.

Hamada et al. teaches a pharmaceutical composition comprising a cyclodextrin inclusion complex of taxol (abstract). Hamada et al. teaches said complex prepared and used as an aqueous solution (column 3, lines 20-30 and column 4, lines 54-56). Hamada et al. teaches optimization of the dosage is within the level of one of the ordinary skill in the art (column 4, lines 44-47).

It would have been obvious to one of ordinary skill in the art to combine Ortiz-Mellet et al. in view of Kotter et al. and Hamada et al. Both Ortiz-Mellet et al. and Hamada et al. are in the field of the use of cyclodextrin inclusion complex of a taxol as a drug delivery system. Both Ortiz-Mellet et al. and Hamada et al. teach the improved solubility of a cyclodextrin inclusion complex of a taxol. (Ortiz-Mellet, page 1989, left

column, paragraph 1; and Hamada, abstract). It would have been routine to one of ordinary skill in the art to formula a drug delivery system into a pharmaceutical composition. The limitation of instant claim 43, "characterized in that it contains per unit dose approximately 100 mg to approximately 750 mg of one of said complex." (emphasis added) is interpreted as an intended use of the instantly claimed pharmaceutical composition used to formulate a unit dose, not a structural limitation of said pharmaceutical composition. It is apparent from what is disclosed that the pharmaceutical composition taught by Ortiz-Mellet et al. in view of Kotter et al. and further in view of Hamada et al. is inherently capable of being formulated into a unit dose containing 100 mg to approximately 750 mg of one of said complex, meeting the functional limitation of instant claim 43. Further, Hamada et al. teaches that routine optimization of the dosage is within the level of one of the ordinary skill in the art.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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